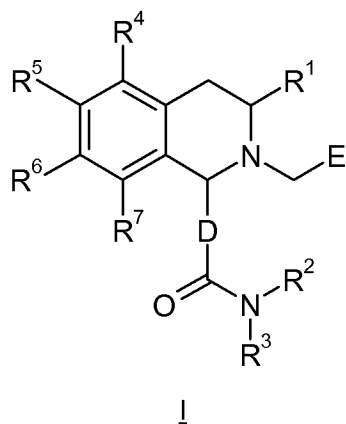


In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claims

1. (original) A compound of formula I, a pharmaceutically acceptable salt thereof, diastereomers, enantiomers, or mixtures thereof:



wherein

R^1 is selected from $-H$ and C_{1-6} alkyl;

R^2 and R^3 are independently selected from $-H$ and C_{1-6} alkyl;

R^4 , R^5 , R^6 and R^7 are independently selected from $-H$, $-OH$, halogen, $-NO_2$, C_{1-6} alkyl, C_{6-10} aryl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, C_{3-6} heterocyclyl-oxy, C_{3-6} heterocyclyl- C_{1-4} alkoxy, C_{6-10} aryl-oxy, C_{6-10} aryl- C_{1-4} alkoxy, C_{1-6} alkyl- $S(=O)_2$ -O-, C_{6-10} aryl- $S(=O)_2$ -O-, C_{1-6} alkyl-NH- $S(=O)_2$ -O-, and $(C_{1-6}alkyl)_2N-S(=O)_2$ -O-; or any two adjacent groups selected from R^4 , R^5 , R^6 and R^7 form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C_{1-6} alkyl, C_{6-10} aryl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, C_{3-6} heterocyclyl-oxy, C_{3-6} heterocyclyl- C_{1-4} alkoxy, C_{6-10} aryl-oxy, C_{6-10} aryl- C_{1-4} alkoxy, C_{1-6} alkyl- $S(=O)_2$ -O-, C_{6-10} aryl- $S(=O)_2$ -O-, C_{1-6} alkyl-NH- $S(=O)_2$ -O-, and $(C_{1-6}alkyl)_2N-S(=O)_2$ -O- are optionally substituted with one or more groups selected from halogen, C_{1-3} alkoxy, $-OH$, $-NO_2$, C_{1-3} alkyl, $-NH_2$, and $-CO_2$ - C_{1-3} alkyl;

E is a 5-membered heterocyclyl optionally substituted with one or more groups selected from halogen, C_{1-6} alkyl, $-C(=O)$ -O- C_{1-6} alkyl, C_{6-10} aryl, C_{6-10} aryl- C_{1-4} alkyl, and C_{6-10} aryl- $S(=O)_2$; and

D is a divalent group comprising a benzene ring.

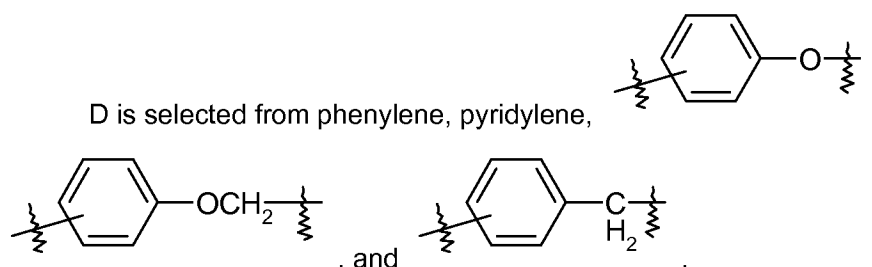
2. (original) A compound according to claim 1, wherein

R^1 is selected from $-H$ and C_{1-3} alkyl;

R^2 and R^3 are independently C_{1-3} alkyl;

R^4 , R^5 , R^6 and R^7 are independently selected from $-H$, $-OH$, halogen, $-NO_2$, C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, tetrahydropyranyloxy, pyridinyloxy, morpholinyl, tetrahydropyranyl- C_{1-4} alkoxy, pyridinyl- C_{1-4} alkoxy, morpholinyl- C_{1-4} alkoxy, phenoxy, benzyloxy, C_{1-6} alkyl- $S(=O)_2-O-$, phenyl- $S(=O)_2-O-$, C_{1-3} alkyl-NH- $S(=O)_2-O-$, and $(C_{1-3}alkyl)_2N-S(=O)_2-O-$; or any two adjacent groups selected from R^4 , R^5 , R^6 and R^7 form a divalent group selected from $-O-CH_2-O-$ and $-O-CH_2-CH_2-O-$, wherein said C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, tetrahydropyranyloxy, pyridinyloxy, morpholinyl, tetrahydropyranyl- C_{1-4} alkoxy, pyridinyl- C_{1-4} alkoxy, morpholinyl- C_{1-4} alkoxy, phenoxy, benzyloxy, C_{1-6} alkyl- $S(=O)_2-O-$, phenyl- $S(=O)_2-O-$, C_{1-3} alkyl-NH- $S(=O)_2-O-$, and $(C_{1-3}alkyl)_2N-S(=O)_2-O-$ are optionally substituted with one or more groups selected from halogen, methoxy, $-OH$, $-NO_2$, and C_{1-3} alkyl;

E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more groups selected from halogen, C_{1-4} alkyl, $-C(=O)-O-C_{1-3}$ alkyl, phenyl, benzyl, and benzenesulfonyl; and



3. (original) A compound according to claim 1, wherein

R^1 is selected from $-H$ and methyl;

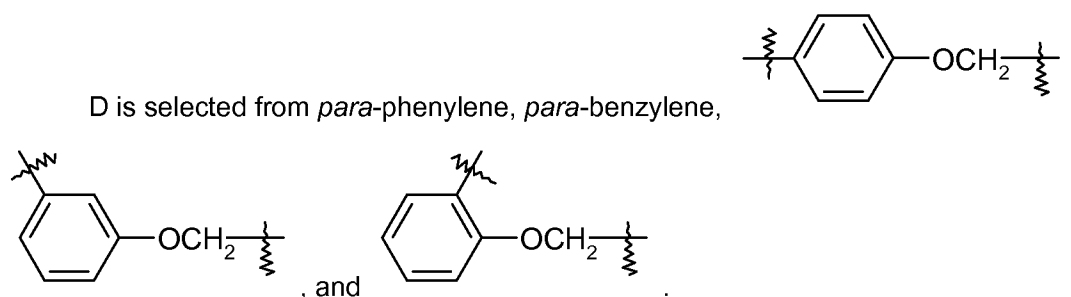
R^2 and R^3 are selected from ethyl and isopropyl;

R^4 , R^5 and R^6 are independently selected from $-H$, $-OH$, halogen, $-NO_2$, C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, tetrahydropyranyloxy, pyridinyloxy, morpholinyl, tetrahydropyranyl- C_{1-4} alkoxy, pyridinyl- C_{1-4} alkoxy, morpholinyl- C_{1-4} alkoxy, phenoxy, benzyloxy, C_{1-6} alkyl- $S(=O)_2-O-$, phenyl- $S(=O)_2-O-$, C_{1-3} alkyl-NH- $S(=O)_2-O-$, and $(C_{1-3}alkyl)_2N-S(=O)_2-O-$; or any two adjacent groups selected from R^4 , R^5 and R^6 form $-O-CH_2-O-$, wherein said phenoxy, benzyloxy, and phenyl- $S(=O)_2-O-$ are optionally substituted with one or more groups selected from halogen and methoxy;

R^7 is selected from $-H$ and C_{1-3} alkoxy;

E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more

groups selected from halogen, C₁₋₄alkyl, -C(=O)-O-C₁₋₃alkyl, phenyl, benzyl, and benzenesulfonyl; and



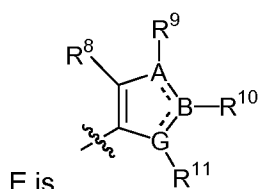
4. (original) A compound according to claim 1, wherein

R¹ is selected from -H and methyl;

R² and R³ are ethyl;

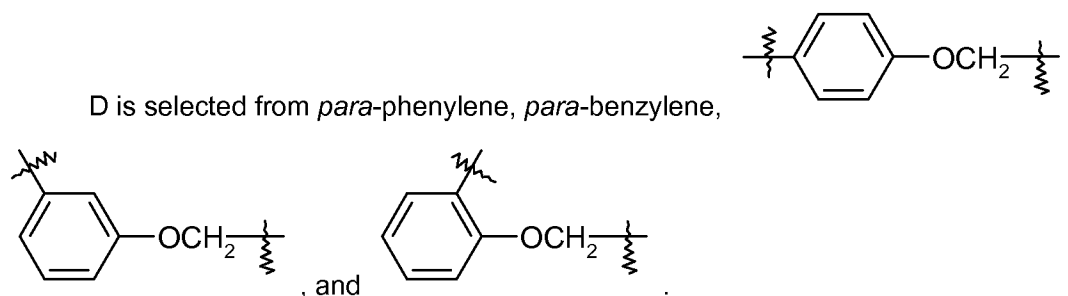
R⁴ is selected from -H, NO₂ and methoxy, R⁵ is selected from -H, -Br, -F, -OH, methoxy, methylsulfonyloxy, N,N-dimethylsulfamoyloxy, and R⁶ is selected from -H, -OH, -NO₂, methoxy, ethoxy, isopropoxy, neopentyloxy, cyclobutyloxy, 4-tetrahydro-2H-pyran-2-yloxy, 2-(4-morpholino)ethoxy, benzyloxy, phenoxy, 4-fluorophenoxy, 3-methoxyphenoxy, 4-methoxyphenoxy, 3-pyridinyloxy, methanesulfonyloxy, benzenesulfonyloxy, dimethylsulfamoyloxy; or any two adjacent groups selected from R⁴, R⁵ and R⁶ form -O-CH₂-O-;

R⁷ is selected from -H and methoxy;



and G is selected from C, N, O and S with a proviso that at least one of A, B and G is C, at most one of A, B and G is S and one of the bonds between A and B, and between B and G is a double bond;

wherein R⁸ is selected from -H, -Cl, methyl, -CO₂Me and phenyl; R⁹ is selected from -H and methyl; R¹⁰ is selected from -H, methyl, n-butyl and phenyl; R¹¹ is selected from -H, methyl, benzyl and benzenesulfonyl.



5. (original) A compound selected from:

COMPOUND 12.1.1: N,N-Diethyl-2-[[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy]benzamide

COMPOUND 12.1.2: 2-[[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy]-N,N-diethylbenzamide

COMPOUND 12.1.3: N,N-Diethyl-3-[[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy]benzamide

COMPOUND 12.1.4: 3-[[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy]-N,N-diethylbenzamide

COMPOUND 12.1.5: N,N-Diethyl-4-[[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy]benzamide

COMPOUND 12.1.6: 4-[[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy]-N,N-diethylbenzamide

COMPOUND 12.1.7: 2-([6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy)-N,N-diethylbenzamide

COMPOUND 12.1.8: 4-([6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]methyl)-N,N-diethylbenzamide

COMPOUND 12.1.9: 4-{6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.10: N,N-Diethyl-4-{6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.11: N,N-Diethyl-4-{7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.12: N,N-Diethyl-4-{2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.13: 4-{2-[(2-Butyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.14: 4-{2-[(2-Butyl-4-chloro-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.15: 4-{6,7-Dimethoxy-2-[(2-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.16: 4-{6,7-Dimethoxy-2-[(3-phenyl-1H-pyrazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.17: 4-{6,7-Dimethoxy-2-[[1-(phenylsulfonyl)-1H-pyrrol-2-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.18: N,N-Diethyl-4-{2-[(2-ethyl-4-methyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.19: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.20: 4-{5,8-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.21: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 12.1.22: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.23: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.24: 4-{6,7-Dimethoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.25: N,N-Diethyl-4-{6-methoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.26: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.27: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.28: 4-{2-[(1-Benzyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.29: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.30: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.31: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methoxy)-N,N-diethylbenzamide

COMPOUND 12.1.32: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methyl)-N,N-diethylbenzamide

COMPOUND 12.1.33: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

COMPOUND 12.1.34: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

COMPOUND 12.1.35: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.36: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.37: 4-{2-[(2,5-Dimethyl-1,3-thiazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.38: 4-{6,7-Dimethoxy-2-[(2-phenyl-1,3-thiazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.39: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.40: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(2-morpholin-4-ylethoxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.41: 4-{7-Ethoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.42: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.43: N,N-Diethyl-4-{6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.44: N,N-Diethyl-4-{7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.45: Methyl 5-{[1-{4-[(diethylamino)carbonyl]phenyl}-6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl]methyl}-1H-imidazole-4-carboxylate

COMPOUND 12.1.46: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl methanesulfonate

COMPOUND 12.1.47: N,N-Diethyl-4-{6-[(4-methyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

COMPOUND 12.1.48: N,N-Diethyl-4-{6-[(2-phenyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

COMPOUND 12.1.49: 4-{6-Bromo-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.50: 4-{6-Bromo-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.51: 4-{6,7-Dimethoxy-3-methyl-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.52: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.53: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-7-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.54: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-5-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.55: N,N-Diethyl-4-{7-[(4-methyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.56: N,N-Diethyl-4-{7-[(2-phenyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.57: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.58: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.59: 4-{7-(Cyclobutyloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.60: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(neopentyloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.61: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.62: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.63: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl dimethylsulfamate

COMPOUND 13.1.1: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(tetrahydro-2H-pyran-4-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 14.1.1: N,N-Diethyl-4-{6-methoxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.2: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.3: N,N-diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.4: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.5: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.6: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(pyridin-3-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 15.1.1: 4-{7-(Benzyloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 16.4.1: N,N-Diethyl-4-{6-methoxy-7-(3-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.2: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.3: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl benzenesulfonate

COMPOUND 17.1.1: 4-{6,7-Dihydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 17.1.2: N,N-Diethyl-4-{6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.3: N,N-Diethyl-4-{7-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.4: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 17.1.5: N,N-Diethyl-4-{7-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.6: N,N-Diethyl-4-{6-hydroxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.7: N,N-Diethyl-4-{6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.8: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.9: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 18.1.1: 4-{2-[(1,4-Dimethyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 18.1.2: 4-{2-[(1,5-Dimethyl-1H-imidazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 19.1.1: 4-{7-Ethoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.1.1: 4-((1S)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)-N,N-diethylbenzamide

COMPOUND 20.2.1: 4-((1R)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)-N,N-diethylbenzamide

COMPOUND 20.1.2: N,N-Diethyl-4-((1S)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.2: N,N-Diethyl-4-((1R)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.3: N,N-Diethyl-4-((1S)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.3: N,N-Diethyl-4-((1R)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.4: N,N-Diethyl-4-((1S)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.4: N,N-Diethyl-4-((1R)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.5: N,N-Diethyl-4-((1S)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.5: N,N-Diethyl-4-((1R)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.6: N,N-Diethyl-4-((1S)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.6: N,N-Diethyl-4-((1R)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.7: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

COMPOUND 20.2.7: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

COMPOUND 20.1.8: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

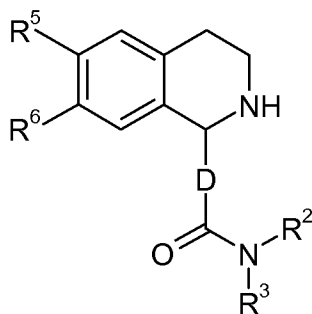
COMPOUND 20.2.8: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide;

and pharmaceutically acceptable salts thereof.

6-7. (cancelled)

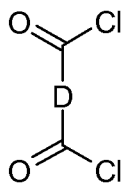
8. (currently amended) A pharmaceutical composition comprising a compound according to claim 1~~any one of claims 1-5~~ and a pharmaceutically acceptable carrier.
9. (currently amended) A method for the therapy of pain in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to ~~any one of claims 1-5~~claim 1.
10. (currently amended) A method for the therapy of functional gastrointestinal disorders in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to ~~any one of claims 1-5~~claim 1.

11. (original) A process for preparing a compound of formula II,

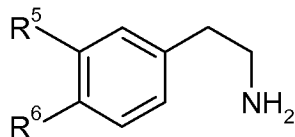


II

comprising of the step of reacting a compound of formula III with a compound of formula IV in the presence of HNR^2R^3 :



III



IV

wherein

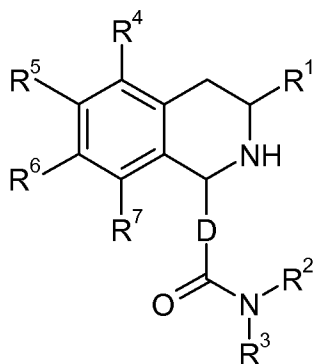
R^2 and R^3 are independently selected from $-\text{H}$ and $\text{C}_{1-6}\text{alkyl}$;

R^5 and R^6 are independently selected from $-\text{H}$, $-\text{OH}$, halogen, $-\text{NO}_2$, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{6-10}\text{aryl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{3-6}\text{cycloalkoxy}$, $\text{C}_{3-6}\text{heterocyclyl-oxy}$, $\text{C}_{3-6}\text{heterocyclyl-C}_{1-4}\text{alkoxy}$, $\text{C}_{6-10}\text{aryl-oxy}$, $\text{C}_{6-10}\text{aryl-C}_{1-4}\text{alkoxy}$, $\text{C}_{1-6}\text{alkyl-S(=O)}_2\text{-O-}$, $\text{C}_{6-10}\text{aryl-S(=O)}_2\text{-O-}$, $\text{C}_{1-6}\text{alkyl-NH-S(=O)}_2\text{-O-}$,

and $(C_{1-6}alkyl)_2N-S(=O)_2-O-$; or R^5 and R^6 together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said $C_{1-6}alkyl$, $C_{6-10}aryl$, $C_{1-6}alkoxy$, $C_{3-6}cycloalkoxy$, $C_{3-6}heterocyclyl-oxy$, $C_{3-6}heterocyclyl-C_{1-4}alkoxy$, $C_{6-10}aryl-oxy$, $C_{6-10}aryl-C_{1-4}alkoxy$, $C_{1-6}alkyl-S(=O)_2-O-$, $C_{6-10}aryl-S(=O)_2-O-$, $C_{1-6}alkyl-NH-S(=O)_2-O-$, and $(C_{1-6}alkyl)_2N-S(=O)_2-O-$ are optionally substituted with one or more groups selected from halogen, $C_{1-3}alkoxy$, $-OH$, $-NO_2$, $C_{1-3}alkyl$, $-NH_2$, and $-CO_2-C_{1-3}alkyl$; and

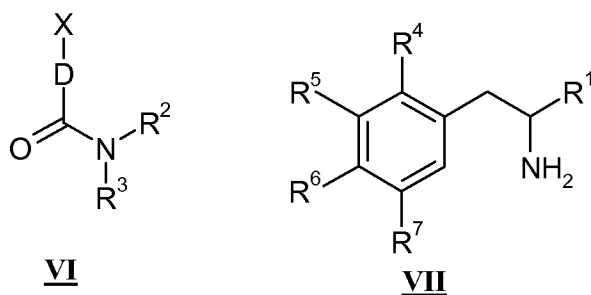
D is a divalent group comprising a benzene ring.

12. (original) A process for preparing a compound of formula V,



V

comprising of the step of reacting a compound of formula VI with a compound of formula VII in the presence of an acid catalyst:



VI

VII

wherein

X is selected from $-CH(OEt)_2$, $=CHOMe$ and $-CHO$;

R^1 is selected from $-H$ and $C_{1-6}alkyl$;

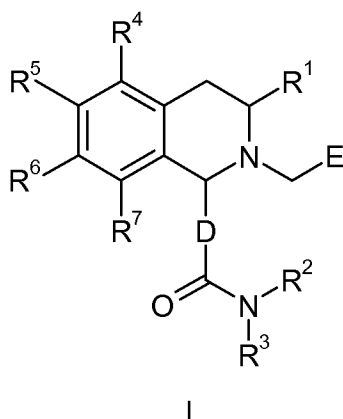
R^2 and R^3 are independently selected from $-H$ and $C_{1-6}alkyl$;

R^4 , R^5 , R^6 and R^7 are independently selected from $-H$, $-OH$, halogen, $-NO_2$, $C_{1-6}alkyl$, $C_{6-10}aryl$, $C_{1-6}alkoxy$, $C_{3-6}cycloalkoxy$, $C_{3-6}heterocyclyl-oxy$, $C_{3-6}heterocyclyl-C_{1-4}alkoxy$, $C_{6-10}aryl-oxy$, $C_{6-10}aryl-C_{1-4}alkoxy$, $C_{1-6}alkyl-S(=O)_2-O-$, $C_{6-10}aryl-S(=O)_2-O-$, $C_{1-6}alkyl-NH-S(=O)_2-O-$, and $(C_{1-6}alkyl)_2N-S(=O)_2-O-$; or any two adjacent groups selected from R^4 , R^5 , R^6 and R^7 form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I,

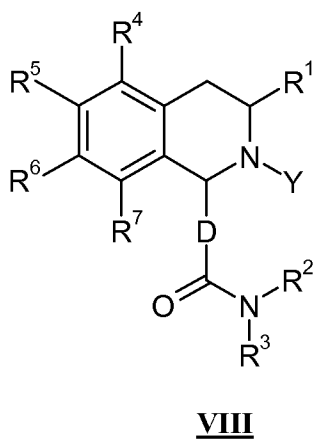
wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocyclyl-oxy, C₃₋₆heterocyclyl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl; and

D is a divalent group comprising a benzene ring.

13. (original) A process for preparing a compound of formula I,



comprising: reacting a compound of formula VIII with E-CHO:



wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R¹ is selected from -H and C₁₋₆alkyl;

R² and R³ are independently selected from -H and C₁₋₆alkyl;

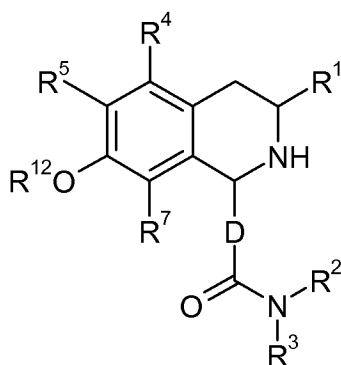
R⁴, R⁵, R⁶ and R⁷ are independently selected from -H, -OH, halogen, -NO₂, C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocyclyl-oxy, C₃₋₆heterocyclyl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O-; or any two adjacent groups selected from R⁴, R⁵, R⁶ and R⁷

form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocyclyl-oxy, C₃₋₆heterocyclyl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl;

E is a 5-membered heterocyclyl optionally substituted with one or more groups selected from halogen, C₁₋₆alkyl, -C(=O)-O-C₁₋₆alkyl, C₆₋₁₀aryl, C₆₋₁₀aryl-C₁₋₄alkyl, and C₆₋₁₀aryl-S(=O)₂-; and

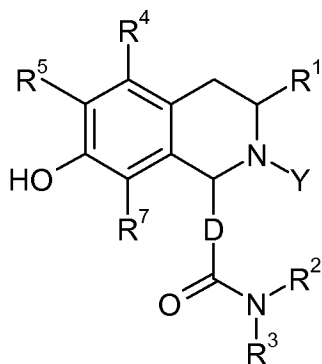
D is a divalent group comprising a benzene ring.

14. (original) A process for preparing a compound of formula IX,



IX

comprising: reacting a compound of formula X with R¹²-OH or R¹²-B(OH)₂:



X

wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R¹² is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₆₋₁₀aryl-C₁₋₄alkyl, C₃₋₆heterocyclyl-C₁₋₄alkyl, C₆₋₁₀aryl, and C₃₋₆heteroaryl, wherein said C₆₋₁₀aryl, C₃₋₆heterocyclyl and C₃₋₆heteroaryl

are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂ and -CO₂-C₁₋₃alkyl; and

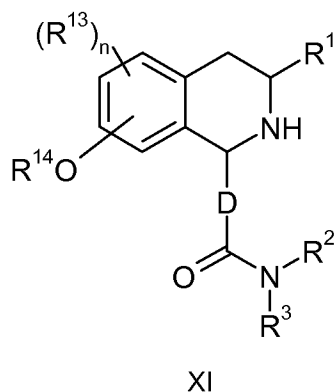
R¹ is selected from -H and C₁₋₆alkyl;

R² and R³ are independently selected from -H and C₁₋₆alkyl;

R⁴, R⁵, and R⁷ are independently selected from -H, -OH, halogen, -NO₂, C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocyclyl-oxy, C₃₋₆heterocyclyl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O-; or R⁴ and R⁵ together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocyclyl-oxy, C₃₋₆heterocyclyl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl; and

D is a divalent group comprising a benzene ring.

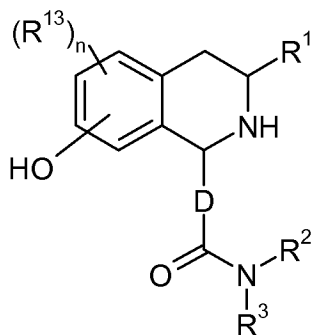
15. (original) A process for preparing a compound of formula XI,



comprising:

reacting a compound of formula XII with NsCl, NsBr, or (CF₃CO)₂O to protect the =NH group of formula XI;

reacting the protected compound with R¹⁴-Y¹ followed by deprotecting the =NH group:



XII

wherein

n is 0, 1, 2 or 3;

each R^{13} is independently selected from $-H$, $-OH$, halogen, $-NO_2$, C_{1-6} alkyl, C_{6-10} aryl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, C_{3-6} heterocyclyl-oxy, C_{3-6} heterocyclyl- C_{1-4} alkoxy, C_{6-10} aryl-oxy, C_{6-10} aryl- C_{1-4} alkoxy, C_{1-6} alkyl- $S(=O)_2-O-$, C_{6-10} aryl- $S(=O)_2-O-$, C_{1-6} alkyl-NH- $S(=O)_2-O-$, and $(C_{1-6}alkyl)_2N-S(=O)_2-O-$; or any two adjacent R^{13} form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C_{1-6} alkyl, C_{6-10} aryl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, C_{3-6} heterocyclyl-oxy, C_{3-6} heterocyclyl- C_{1-4} alkoxy, C_{6-10} aryl-oxy, C_{6-10} aryl- C_{1-4} alkoxy, C_{1-6} alkyl- $S(=O)_2-O-$, C_{6-10} aryl- $S(=O)_2-O-$, C_{1-6} alkyl-NH- $S(=O)_2-O-$, and $(C_{1-6}alkyl)_2N-S(=O)_2-O-$ are optionally substituted with one or more groups selected from halogen, C_{1-3} alkoxy, $-OH$, $-NO_2$, C_{1-3} alkyl, $-NH_2$, and $-CO_2-C_{1-3}alkyl$;

Y^1 is halogen;

R^{14} is selected from $C_{1-6}alkyl-S(=O)_2-$, $C_{6-10}aryl-S(=O)_2-$, $C_{1-6}alkyl-NH-S(=O)_2-$, and $(C_{1-6}alkyl)_2N-S(=O)_2-$;

R^1 is selected from $-H$ and $C_{1-6}alkyl$;

R^2 and R^3 are independently selected from $-H$ and $C_{1-6}alkyl$; and

D is a divalent group comprising a benzene ring.

16. (new) A method for the therapy of anxiety in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to claim 1.